

In the Specification

Applicants present replacement paragraphs below indicating the changes with insertions indicated by underlining and deletions indicated by strikeouts and/or double bracketing.

Please replace the paragraph beginning at page 13, line 2 with the amended paragraph as follows. Support for this amendment may be found at least within this paragraph and in FIGS. 1-2.

The methods of the invention are based on time-correlated measurements of elongated polymers as they travel past two or more detection zones which are spaced apart by known, pre-determined distances. A schematic illustration of one embodiment of the apparatus of the invention is presented in FIG. 1. For example, detection zones 101 and 102 are separated by a distance represented as D1. The corresponding time-correlated signal amplitude profiles 106 and 107 shown in FIG. 2 are temporally separated by the time the polymer (105) takes to travel the distance D1 between the detection zones. As the polymer passes each detection zone, a signal amplitude profile is generated. These are depicted schematically in FIG. 2, in which the polymer 105 first passes detection zone 101 which generates profile 106, then passes detection zone 102 which generates profile 107, and finally passes detection zone 103 ~~[[102]]~~ which generates profile 108. Signal amplitude profiles are then used to determine the velocity of the polymer. Of course, the invention is not intended to be limited to the use of three detection zones. Rather, as few as ~~[[a]]~~ two detection zones may be employed, while the maximum number of such zones is virtually unlimited.

Please replace the paragraph beginning at page 13, line 30 with the amended paragraph as follows. Support for this amendment may be found at least within this paragraph.

Distances among detection zones can be determined using any methods known in the art. In one embodiment, the distances are measured by ~~[[a]]~~ mechanical systems that offer high spatial resolution. In another embodiment, the distances can be measured by calibration using elongated polymers of a known length. In still another embodiment, the distances can be

measured by calibration using a fluid flow of known velocity. Such calibration methods are well known in the art.

Please replace the paragraph beginning at page 14, line 8 with the amended paragraph as follows. Support for this amendment may be found at least within this paragraph.

In FIG. 3, various velocity measurements are represented for first 201 and second 202 signal amplitude profiles measured at first and second detection zones. Various time intervals, used ~~[[use]]~~ for the velocity determination, are depicted in FIG. 3 as well.

Please replace the paragraph beginning at page 16, line 5 with the amended paragraph as follows. Support for this amendment may be found at least within this paragraph.

The signal measured at the detection zone can also be light scattered by a polymer labeled with molecules having light-scattering properties. As noted above, a laser beam of a selected wavelength can be used to define the detection zone or, alternately, a slit of select width is used to define the detection zone.

Please replace the paragraph beginning at page 19, line 6 with the amended paragraph as follows. Support for this amendment may be found at least within the equations following this paragraph on page 19.

where $v(t)$ is the velocity of the polymer at time t . Thus the temporal location of the center-of-mass t_{com} ~~[[tcom]]~~ of an elongated polymer can be determined by solving the equation

Please replace the paragraph beginning at page 26, line 4 with the amended paragraph as follows. Support for this amendment may be found at least within this paragraph and in particular on page 26, line 7.

The detection zones were laser spots formed by an argon ion laser running at 488 nm and delivering about 2 mW of laser power to each of the spots. The spots were diffraction limited, with a spot size of approximately 0.5 microns in diameter. The laser spots were spaced 15 mm apart and located within the nanochannel in the path of the DNA molecules. A carrier liquid containing labeled DNA was flowed through the nanochannel in a manner such that laminar flow lines allowed the DNA to be delivered through the two laser spot detection zones. The DNA molecules comprised -DNA that was intercalated with YOYO-1 at a final concentration of one YOYO-1 molecule/10 base-pairs. The carrier solution contained 100 mM DTT in a 1x TBE solution. A fluid drive, delivering 50 psi, was used to drive the DNA through the channel. The chip was [[been]] sealed using known chemical activation sealing techniques. The surfaces to be bonded (the quartz chip and a quartz coverslip) were activated using an ammonium hydroxide:peroxide:water mixture, heated to 70 °C. The coverslip and the quartz chip were then pressed together under water and the clamped package was baked to evaporate any solvent and cause chemical bonding of the two surfaces. The DNA sample mixture was then introduced into the chip by capillary forces. The signals measured from the two laser excitation spots, arranged 15 mm [[microns]] apart, were collected through a Nikon 1.4 NA 100x oil immersion objective. The resultant fluorescent signals were filtered and detected by two avalanche photodiodes. The signals from the two intercalator signals were then collected through a data capture board, processed through an A/D converter, and stored on a computer. The computer allowed processing of the data and calculation of the lengths of the molecules. A constant velocity estimation was used to derive the velocity of the molecules moving through the system. The velocity was a COM to COM velocity estimation/calculation. The average length of the lambda molecules was measured to be around 18 microns, corresponding to an approximate 20% increase in the length of the DNA molecule from the intercalator staining. The data was processed using an algorithm written in MATLAB data processing language.